71. A recombinant vector comprising the polynucleotide of claim 67, wherein said member is (a) or (b) and said polynucleotide is DNA.

72. A recombinant vector comprising the polynucleotide of claim 67, wherein said member is (a) and said polynucleotide is DNA.

73. A recombinant host cell comprising the polynucleotide of claim 67, wherein said member is (a) or (b) and said polynucleotide is DNA.

74. A method for producing a polypeptide comprising culturing the recombinant cell of claim 73 and expressing the polypeptide encoded by said polynucleotide, wherein said polypeptide produced when it has a sequence other than SEQ ID NO:2 has the ability to bind to a ligand which binds to a polypeptide having the sequence of SEQ ID NO:2.--

Good.

Remarks

Claims 21-54 have been cancelled without prejudice and new claims 55-74 have been inserted without prejudice to avoid any issues under new PTO policy with regard to claims that include the term "identity" as a discriptor. The claims of the above amendment are believed to be fully supported by the original claims, specification or drawings. Therefore, no new matter is believed to be presented. Further, pages 6-14 of the specification provide

examples of descriptive support for the newly submitted alternative claim language. Such issue will be discussed below after a dissussion of the mature polypeptide structures and the functional language in the polypeptide production claims.

In view of the April 2, 1998 Office Action and conversations with the PTO, the above amendment is being submitted to place the present application in condition for allowance. Since the PTO has shifted its position on claims that use the term "identity" in polynucleotide claims and now asserts a 35 U.S.C. §112, second paragraph, rejection against them, the above amendment is submitted to simply avoid such an issue entirely and expedite the prosecution of the present application.

The Term Mature relates to Peptides With and Without the N-terminal Methionine)

Certain claims are objected to by the Examiner due to their utilization of term mature. Such term refers to *inter alia* the amino acid sequence phrase "amino acids 2 to 352 of SEQ ID NO:2" and the corresponding nucleotide sequence phrase describing the sequence encoding the amino acid sequence. This objection and rejection should be withdrawn since the above phrase has been substituted for the word mature in the new present.

The legal standard for "written description" is discussed extensively in Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991):

> A fairly uniform standard for determining compliance with the "written description" requirement has been maintained throughout: "Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."
>
> * * *
>
> "The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon 'reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.'"

935 F.2d at 1562-63 (citations omitted).

Under this legal analysis, the support provided by the present specification cannot be determined in a vacuum by reference to the words in the specification alone. Thus, the only issue is whether one of ordinary skill in the art would have reasonably recognized from reading the specification that the inventors were in possession of a polynucleotide encoding amino acids 2-352 of SEQ ID NO:2. As set forth on page 3 of the office action, such polynucleotides are supported by the specification and there is no need to explore the structures for polynucleotides encoding other mature polypeptides other than amino acids 2 to 352 (1 to 352) of

SEQ ID NO:2. Accordingly, this ground of rejection is believed to be overcome and should be withdrawn.

Functional Activity Language in Specification

The polypeptide production claims previously used a funtionaly activity phrase "wherein said polypeptide produced when it has a sequence other than SEQ ID NO:2 has the ability to bind to a ligand which binds to a polypeptide having the sequence of SEQ ID NO:2". Such phrase is fairly conveyed by the language on page 11 of the specification (second full paragraph) and is not new matter. Other locations which support such language are found throughout the specification and the binding assays to which they refer are well-known in the art. Perhaps applicant could have more specifically referred to such locations in the prior response. However, such phrase is fully supported by the specification and is not new matter.

Moreover, in view of the specification and the appended Ruben Declaration assays with such ligands to determine if a particular polypeptide candidate will bind to a ligand which also binds to the polypeptide having a sequence according to SEQ ID NO:2 are routine in the art. Only routine skill and routine testing are required which is not undue experimentation. *See, In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988).

Moreover, ligands that bind to the G-protein chemokine receptor shown in Figure 1 (whose amino acid sequence is SEQ ID NO:2 in the Sequence Listing) are known in the art as ligands for related polypeptides. The polypeptide of SEQ ID NO:2 is described in the paragraph bridging pages 6 and 7 of the specification, as being derived from human monocytes and having at least 70.1% identity to the chemokine receptor (see Figure 2) that binds to the human monocyte chemotractant protein (MCP)-1 ligand (a C-C cytokine ligand that is described in paragraph 5 of the Ruben Declaration, which ligand has since been verified to also bind to the polypeptide of SEQ ID NO:2).

As set forth in the Ruben Declaration, binding assays for ligands to the polypeptide G-protein chemokine receptor having an amino acid sequence as set forth in SEQ ID NO:2 (see Figure 1) have been performed with positive results. Ligands do in fact exist that bind to the receptor according to the invention and some such bindings have been published in the literature after the present application was filed. Such ligands that bind include C-C cytokine ligands which are well-known to be involved in an inflammatory response (see paragraph 5 and 6 of Ruben Declaration). In fact, the human ligands known as (MIP)-1α and (MIP)-1ß are examples of ligands that bind to the G-protein chemokine receptor set forth in Figure 1 (SEQ ID NO:2). Binding of the above ligands (and other ligands) to the above-described receptor or to a particular polypeptide candidate is readily verified by procedures set forth

in the above-captioned application and, more particularly, by utilizing techniques well-known and routine in this field.

In particular, utilizing a detectable form of the receptor (see page 27, lines 19-30, of the specification) and investigating the binding of such receptor to ligands involved in an inflammatory response as referred to on page 3, line 12, through page 4, line 15 of the specification (see paragraphs 2 and 3, above), including known ligands involved in the inflammatory response that are recognized in this field as being members of the C-C chemokine family (see paragraphs 5 and 6, above), readily results in binding of either MIP-1α or MIP-1ß to the receptor.

Once such ligand is bound (as described above) and the bound receptor/ligand complex is detected, the complex is readily isolated using methods well-known in the art. The ligand may then be separated from the receptor/ligand complex and labelled to permit further investigation of receptor and ligand binding (see paragraph bridging pages 21-22 of specification). Utilizing the labelled ligand obtained as described above, the effects of receptor analogs, ligand analogs, antagonists or agonists on the receptor/ligand binding may be investigated by routine and well-known procedures.

Further, ligand assay procedures are well-known to those in the chemokine receptor/ligand field and are described generally at page

27, lines 19-30, of the specification. Page 27, at lines 28-30, cross-references systems to assay for agonists and/or antagonists to the binding of such receptor to the ligand (such as receptor analogs that also bind the ligand). Such systems are also well-known in this field.

Other uses for the present polypeptide are reasonably inferred from its structure, location and similarity to other proteins. For example, on page 3, in the last 10 lines of the page, the above-captioned application states that many chemokines and their receptors (including chemokine receptors similar to the chemokine receptor of Figure 1 (SEQ ID NO:2)) have pro-inflammatory activity and are involved in multiple steps during an inflammatory reaction.

For the above reasons, the functional ligand-binding term currently utilized as a limitation in the polypeptide production claims is fully supported by the original specification and provides a process for making useful polypeptides. Further, the assay to screen for such activity is well within the skill of the ordinary practitioner in this field. Accordingly, this ground of rejection is overcome and should be withdrawn.

New Claim Format is Fully Supported by the Specification

The claims of the above amendment are believed to be fully supported by the original claims, specification or drawings.

Therefore, no new matter is believed to be presented. Further, pages 6-14 of the specification provide examples of descriptive support for the newly submitted alternative claim language.

The previously submitted polynucleotide claims utilized the term "identity" with regard to polynucleotide variants and polypeptides encoded by some of said variants. Applicant is providing the above substitute claims (without prejudice) merely to expedite prosecution and proceedings at the PTO. Applicant does not agree with or acquiesce to the PTO's current policy with regard to the term "identity" in claims to polynucleotides. However the above claims utilize an alternative claim format which focuses the facts that the variants are obtained from inserting, deleting and/or substituting nucleotides into a given useful sequence and that the varaint thus obtained will hybridize with the complement of the useful polynucleotide. Therefore, the term "identity" is not found in the present claims.

Claims 55-74 are presented without prejudice merely to expedite the prosecution of this application and simplify examination by clarifying the elected subject matter. Applicant is of the firm position that the term "identity" is clear in the context of the present specification in view of the state of the art. However, new alternative claims are presented above that clearly describe the present invention as described in the specification. In fact, the present specification makes clear that any reading of a phrase

such as "at least 95% identity" must be understood to have less than or equal to 5% differences between two aligned sequences along a specific stretch of the nucleotides (which are very close to one another in length, *i.e.*, no more than 5% length variations) because of the dual stringent hybridization and identity requirements.

As is clear from the record, the reference sequence (polynucleotide coding sequence encoding the polypeptide of SEQ ID NO:2, with or without the N-terminal methionine) is utilized as a starting reference point and is varied to provide variant polynucleotides that are useful as probes. For example, the specification (as set forth in the above claims) describes at pages 6-14 (particularly, page 8) variant polynucleotide sequences that are formed by deletion, substitution or insertion of nucleotides into the reference sequence. By one of these three variations (or a combination thereof) a sequence is provided which is at least 95% identical to the reference sequence, *i.e.*, having not more than a 5% difference in nucleotides as described and claimed above. Furthermore, such variant polynucleotides will hybridize under stringent conditions with the complement of the polynucleotide from which they are obtained.

Clearly, the presently claimed variant polynucleotides are now adequately defined in terms that can be readily understood by one of ordinary skill in the art. The number of substituted, deleted, or inserted nucleotides (different nucleotides) in the variant

polynucleotide coding sequence are of no consequence so long as the variant polynucleotide and the complement of the useful polynucleotide from which it was obtained will hybridize under stringent conditons. If the variant polynucleotide will not hybridize with such complement then it is not within the scope of the present claims.

Of course, changes to the reference coding nucleotides that result in only conservative changes to an encoded polypeptide for the variant polynucleotide are preferred. However, regardless of the coding of the variant polynucleotide the fact that it hybridizes with the complement would result in a useful probe for the complement to the starting polynucleotide. There is no doubt that such a polynucleotide would hybridize to the complement of the starting polynucleotide since the claims require it.

Accordingly, in view of the above remarks, the above claims are believed to fully resolve any issues of clarity with regard to the scope for such variant polynucleotides. Therefore, any potential ground of object to the term "identity" is believed to be obviated and the present claims are simplified.

Further, the rejection over prior art under 35 U.S.C. §102(b) is deemed moot in view of the above amendment. The rejection was only asserted since the Examiner interpreted the claims as being vague and thought that the claim might be read broadly enough to

include the unrelated polynucleotide of the cited reference. However, the above claims avoid any such overlap and clearly overcome such a rejection.

There is no basis in patent law to require a second utility for the hybridization probe variants, in that the polynucleotide hybridization probes must also encode a polypeptide having all the biological properties and activities of the polypeptide of SEQ ID NO:2. Further, it is not clear why the described usefulness for hybridization (which inherently makes it useful as a probe to isolate a useful polynucleotide) would not deemed by the Examiner to be an adequate utility for purposes of patentability.

Since the claims, as amended are free of the prior art and in view of the above amendment and remarks, the above claimed invention is believed to be patentable over the prior art of record. An early notice to that effect is urged.

Further applicants' representative reiterates and certifies by the signature below the following:

The culture of ATCC 97183 will be maintained for 30 years after the date of deposit and will be replaced with living cultures if such should become destroyed or defective. Further, if a patent should issue which is directed to the present invention, upon the

issuance of such a patent the deposited strain of ATCC 97183 will be irrevocably and without restriction released to the public.

The Examiner is invited to call the undersigned at the below number if any further action by applicant would expedite the examination of this application.

FIRST CLASS MAIL CERTIFICATE

Deposit date: August 3, 1998.

I hereby certify that this paper and the attachments hereto are being deposited with the U.S. Postal Service "First Class Mail" service under 37 CFR 1.10 on the date indicated above addressed to:

Box Amendment - ~~No~~ Fee Due
Assistant Commissioner for Patents
Washington, DC 20231

J.G. Mullins, Esq. **Date** 8/3/98

Respectfully submitted,

J.G. Mullins, Esq.
Reg. No. 33,073
CARELLA, BYRNE, BAIN, GILFILLAN,
CECCHI, STEWART & OLSTEIN
Six Becker Farm Road
Roseland, NJ 07068
Tel. No.: (201) 994-1700

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